



**Al-Nahrain University
College Of Medicine**



Hyperlipidemia in chronic renal failure

**Research submitted to department of medicine /college of medicine/
Al-Nahrain University as a part of M.B.CH.B graduation requirement**

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2018-2019

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LIST OF ABBREVIATIONS

Symbols	Meanings
CKD	Chronic Kidney Disease
CVD	Cardiovascular disease
NCEP/ ATP	National Cholesterol Program/ Adult Treatment Panel
NICE	National Institute for Clinical Excellence
ESC	The European Society of Cardiology
KDIGO	Kidney Disease Improving Global Outcomes
HDL-C	High Density Lipoprotein Cholesterol
LDL-C	Low Density Lipoprotein Cholesterol
VLDL	very low density lipoprotein
TG	Triglycerides
DM	Diabetes Mellitus
HTN	Hypertension
PCKD	Polycystic Kidney Disease
WHO	World Health Organization

DEDICATION

To My...

Parents,

& Brother

For their ever support...

ACKNOWLEDGEMENT

I would like to express my sincere attitude to my teacher and supervisor Dr. Jawad kadim for his great help, kind and support throughout the period of this study...

Further, I am greatly indebted to Internal Medicine Department team at Al-Nahrain Medical School, whose professional expertise is matched only by their concern to make a researcher task as trouble-free as possible...

Finally, it is with particular pleasure that I express my gratitude to everyone who has helped me in finishing this work in any point of its implementation, conduction and final execution...

ABSTRACT

Introduction:

Chronic kidney disease is characterized by specific metabolic abnormalities of plasma lipoproteins, These abnormalities involve all lipoprotein classes and shows variations depending on the degree of renal impairment.

Patients with chronic kidney disease (CKD) are at an increased risk for cardiovascular disease and have a higher prevalence of hyperlipidaemia than the general population, The risk of cardiovascular disease (CVD) varies depending on the type of lipid abnormalities, the target population, the cause of renal disease and the degree of reduction in glomerular filtration rate (GFR). The majority (58%) of patients die from cardiovascular causes, making CVD the leading cause of death in patients with CKD.

Patients and methods:

This is a descriptive cross sectional study conducted on chronic renal failure individuals attending to Al-Imamain Al- kadhimiya teaching hospital, A total of 20 individuals had been included in the study sample.

Results:

20 individuals were recruited for this study the number of males (12) and females (8), The mean age of the patients was 51.45±3.9 years.

In present study, the most prevalent lipid abnormality was HDL 78% above the target (>1.02 mmol/l) followed by TG 64% above target (<1.7 mmol/l), then non-HDL 57% above target (<3.4 mmol/l) & LDL 50% above target level (<2.6 mmol/l) & 70% of patients use statin.

Conclusion:

The most prevalent abnormality was HDL (78% above the target) followed by TG (64% above the target), then non-HDL (57% above the target) & LDL (50% above target level), No one of the patients fulfill in all the targets levels.

INTRODUCTION

Chronic kidney disease is characterized by specific metabolic abnormalities of plasma lipoproteins, These abnormalities involve all lipoprotein classes and shows variations depending on the degree of renal impairment.⁽¹⁾

Lipoprotein traditionally are classified based on their densities, ranging from chylomicrons to high density lipoprotein cholesterol [HDL-C], and consist of cholesterol, triglycerides, phospholipids, and protein.⁽²⁾

Factors that may contribute to decreased catabolism and clearance of triglyceride-rich apo-B containing lipoproteins include :

- 1.Reduce activity of lipolytic enzyme
- 2.Compositional abnormalities in lipoproteins preventing binding to appropriate receptors .
- 3.Decrease up take of lipoproteins from circulation. ⁽³⁾

Patients with chronic kidney disease (CKD) are at an increased risk for cardiovascular disease and have a higher prevalence of hyperlipidaemia than the general population, The risk of cardiovascular disease (CVD) varies depending on the type of lipid abnormalities, the target population, the cause of renal disease and the degree of reduction in glomerular filtration rate (GFR).⁽⁴⁾ The majority (58%) of patients die from cardiovascular causes, making CVD the leading cause of death in patients with CKD.⁽⁵⁾ patients on dialysis have 10 to 20 times higher cardiovascular mortality rates than the general population.⁽⁶⁾

according to (NCEP) (ATP) III guidelines

indicate that the upper limit of normal for total cholesterol is 240 mg/dL (6.21 mmol/L), low-density lipoprotein (LDL) cholesterol is 130 mg/dL (3.36 mmol/L), triglycerides (TG) is 200 mg/ dL (2.26 mmol/L) and the lower limit for HDL cholesterol is 35 mg/dL (0.91 mmol/L).⁽⁷⁾

The NCEP ATP III suggests that anyone with elevated cholesterol or other forms of hyperlipidaemia should undergo clinical or laboratory evaluation for secondary dyslipidaemias before starting on anti-lipid therapy, As in the ATP III guidelines, all major treatments are based on the levels of TG, LDL and non-LDL cholesterol.⁽⁸⁾

The ATP III reports have identified LDL cholesterol as the primary target for lipid-lowering therapy and have found that lowering LDL cholesterol levels reduce the risk for cardiovascular events.⁽⁹⁾

The target is to achieve TG level <500 mg/dL and suggested treatment is with therapeutic lifestyle changes (which includes diet, weight reduction, increased physical activity and abstinence from alcohol) followed by a fibrate or niacin.⁽¹⁰⁾

According to ESC guidelines

Elevation of total cholesterol and LDL has received most attention, particularly because it can be modified by lifestyle changes and drug. The evidence showing that reducing TC and LDL can prevent CVD is strong and compelling, based on results from multiple randomized controlled trials (RCTs), TC and LDL levels continue therefore to constitute the primary targets of therapy. Besides an elevation of TC and LDL levels, several other types of dyslipidaemia appear to predispose to premature CVD. A particular pattern, termed the atherogenic lipid triad, is more common than others, and consists of the co-existence of increased VLDL remnants manifested as mildly elevated TG, increased LDL particles, and reduced HDL levels. However, clinical trial evidence is limited on the effectiveness and safety of intervening in this pattern to reduce CVD risk; therefore, this pattern or its components must be regarded as optional targets of CVD prevention.⁽¹¹⁾

According to NICE guidelines

The Guideline Development Group (GDG) recommend the use of non-HDL cholesterol rather than LDL cholesterol. Non-HDL cholesterol is total cholesterol minus HDL cholesterol. LDL cholesterol is not directly measured but requires a calculation using a fasting sample and for triglyceride levels to be less than 4.5 mmol/ litre, where as the measurement of non-HDL cholesterol does not. The European guideline considers patients in terms of different levels of risk and targets reflect the different level of risk. The guidance states that in general, total plasma cholesterol should be <5 mmol/L (<190 mg/dL), and LDL cholesterol should be <3 mmol/L (<115 mg/dL). In subjects with higher CVD risk, the treatment goals should be lower.⁽¹²⁾

According to (KDIGO) guidelines

in adults with newly identified CKD, evaluation of a lipid profile (TC, LDL, HDL, and triglycerides) should be performed mainly because of the potential severe hypercholesterolemia or hypertriglyceridemia diagnosis and potential secondary cause establishment. There is no precise evidence on usefulness of the measurement of the lipid status and its potential to improve clinical outcomes,

but the levels of triglyceride >11.3 mmol/L or LDL >4.9 mmol/L may require further evaluation. Thus, follow-up measurement of lipid levels in adults with CKD is not required for the majority of patients especially because clinical benefits of statin treatment are proportional to the baseline coronary risk rather than baseline LDL.

KDIGO guidelines

recommend treatment with a statin or statin/ezetimibe combination in adults aged ≥ 50 years with eGFR < 60 mL/min/1.73 m² who are not treated with chronic dialysis or kidney transplantation (GFR categories G3a–G5).⁽¹³⁾ according to The recent Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines for the management of hyperlipidemia in patients with kidney disease suggest that all adults with CKD should be evaluated for lipid abnormalities. Assessment of hyperlipidemia should include a complete fasting lipid profile with total, LDL and HDL cholesterol, and TG.⁽¹⁴⁾

The recommendation for a statin/ezetimibe combination comes from the ***Study of Heart and Renal Protection, or SHARP trial***. This study randomized 9270 patients >40 years old with CKD to simvastatin 20 mg plus ezetimibe 10 mg daily regardless of baseline LDL-C levels. Patients were eligible if they had more than one creatinine measurement of ≥ 1.7 mg/dL in men or ≥ 1.5 mg/dL in women. The primary outcome of combined MI, coronary death, stroke, or arterial revascularization was reduced by 17% in the treatment group with a 32% mean reduction in LDL-C levels. This came at the expense of a minor excess risk of myopathy (0.2% in the treatment group vs. 0.1% in the placebo group), without any increased risk of hepatitis, gallstones, or excess death from non-vascular causes.⁽¹⁵⁾

AIM:

The aim of this study is hyperlipidemia in chronic renal failure.

PATIENTS AND METHODS

Study Setting & design

This is a descriptive cross-sectional study conducted on chronic renal failure individuals attending Al-Imamain Al- kadhimiyyain teaching hospital during the period from October 2018 to end of February of 2019.

Selection of study sample

Involved those with chronic renal failure who admitted to medical wards , A total of 20 individuals had been included in the study sample.

Base line assessment

Data was collected through a direct interview with the participants. A verbal consent was taken. Thorough information concerning the patient's condition was obtained, via the questionnaire, from the history, physical examination and biochemical investigations

Data collection

Venous blood specimen was withdrawn after an overnight fasting of at least 12 hours.

Lipid profile were measured, in milligrams per deciliter.

Caution had been considered to avoid repetition of the interview with the same patient by looking only for newly registered patients and marking their files during the time of the study.

Study tools

A questionnaire form paper had been developed by direct interview with the patient .

Statistical analysis

Data was entered and analyzed using Microsoft excel program, also the mean and standard deviation was calculated by free online for mean and standard deviation.

RESULTS

Table 1 : Characteristic of patients

Characteristic		Number
Sex	Male	12
	Female	8
Age	Mean	51.45±3.91 years
Underlying cause	DM	9
	HTN	8
	PCKD	1
	Renal agenesis	1
	Neurogenic bladder	1
Duration	1-3 years	11
	4-6years	4
	7-10years	5
Past medical history	DM	6
	HTN	8
	DM+HTN	3
	Negative	0

Table 2 : The mean & standard deviation of lipid profile in study sample

Lipid profile parameters in (mg/dl)	Mean \pm SD
Total cholesterol	164.26\pm13.96
TG	206.49\pm27.21
HDL	38.43\pm4.58
LDL	93.35\pm9.92
VLDL	41.55\pm5.38
Non-HDL	144.30\pm16.31
Athrogenic index	3.48\pm0.73

Table 3 : S.HDL level of patients in study sample

S.HDL(mg/dl)	Frequency	Percentage
<40	14	70%
40-49	3	15%
50-60	1	5%
>60	2	10%

Table 4 : S.LDL level of patients in study sample

S.LDL (mg/dl)	Frequency	Percentage
<70	6	30%
70-99	6	30%
100-129	4	20%
≥130	4	20%

Table 5 : S.TG level of patients in study sample

S.TG (mg/dl)	Frequency	Percentage
<150	7	35%
150-179	2	10%
180-199	4	20%
>200	7	35%

Table 6 : Non-HDL level of patients in the study sample

Non- HDL(mg/dl)	Frequency	Percentage
<100	9	45%
100-129	1	5%
139-159	2	10%
≥160	8	40%

Table 7 : Proportion of patients within lipid profile target

Lipid profile	With target		Above target	
	Frequency	Percentage	Frequency	Percentage
LDL (< 2.6 mmol/ L)	12	60%	8	40%
Non-HDL (<3.4 mmol/L)	10	50%	10	50%
HDL (> 1.02 mmol/L)	8	40%	12	60%
TG (< 1.7 mmol/L)	13	65%	7	35%

Table 8 : Relationship between duration of statin use and lipid profile levels for various measures

Statin use duration	Mean of LDL(mmol/l)	Mean of HDL(mmol/l)	Mean of TG(mmol/l)	Mean Non-HDL(mmol/l)
1-2	2.05	0.82	1.59	2.83
3-4	2.68	1.2	2.78	3.8
5-6	3.4	0.9	3.5	5.12
total	8.13	2.92	7.87	11.75

Table 9 : Athrogenic index level of patients in study sample

Athrogenic index	Frequency	Percentage
<0.1 (low risk)	3	15%
0.1-0.2 (intermediate)	3	15%
>0. 2 (high risk)	14	60%

Figure 1 : % of statin use in 20 study sample

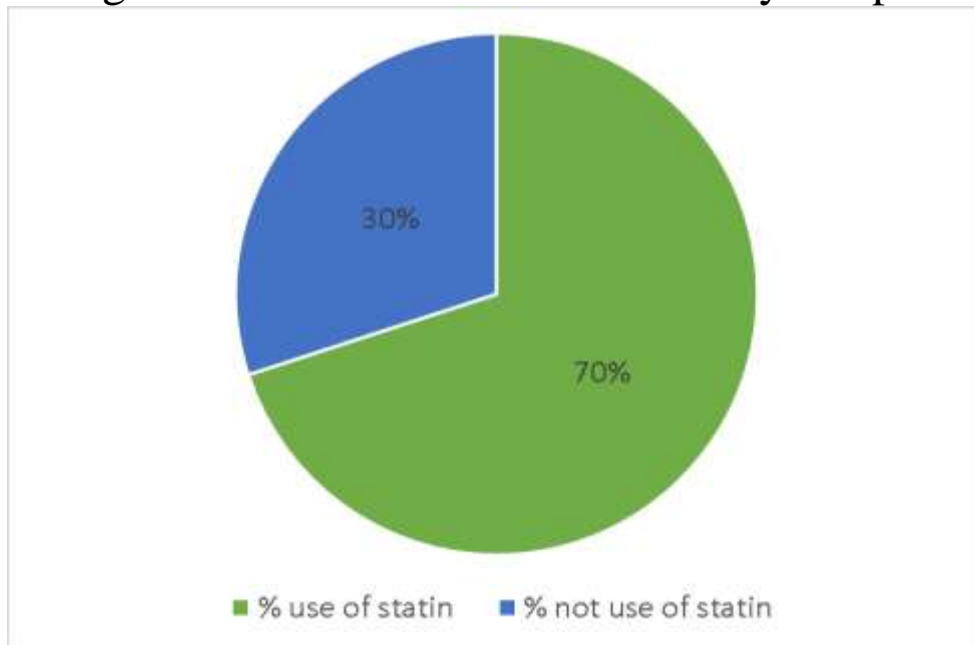


Figure 2 :% of statin use in 12 male study sample

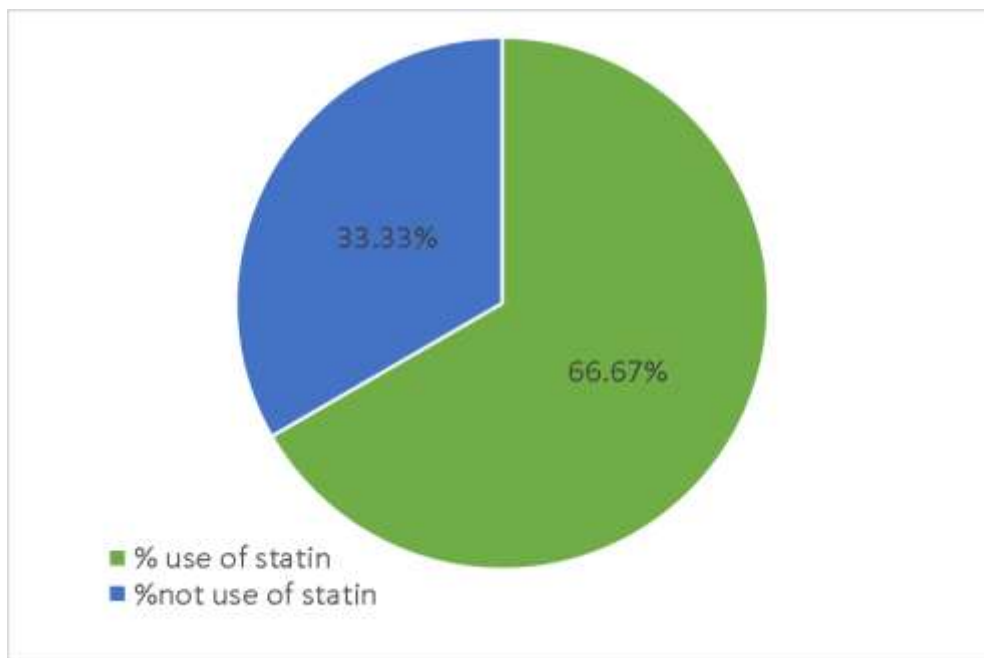


Figure 3 : % statin use in 8 femal study sample

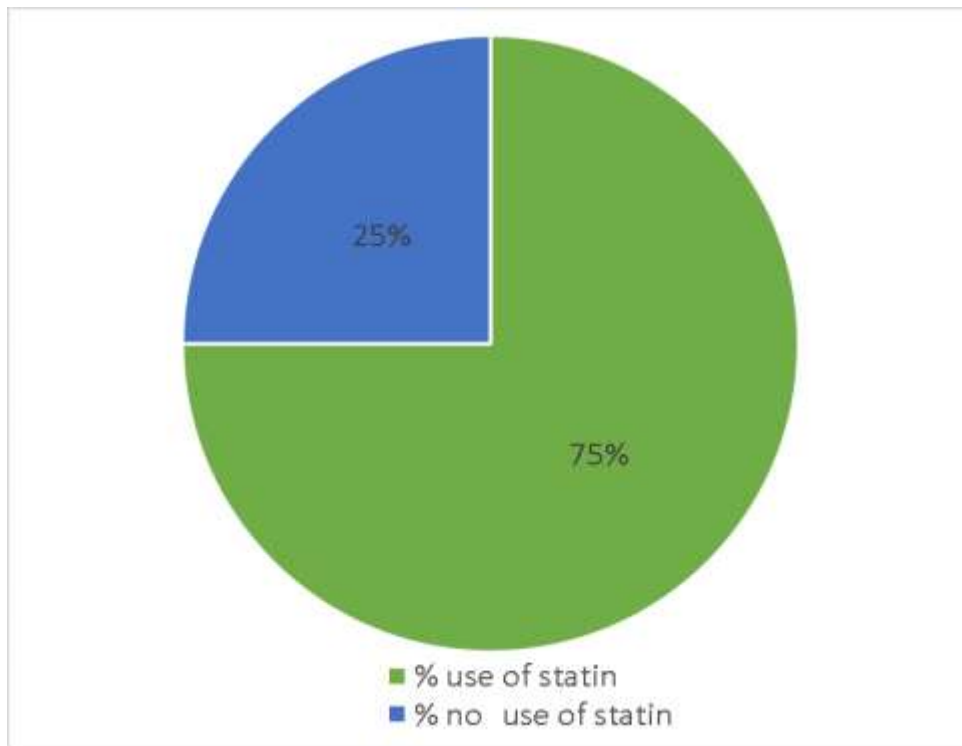
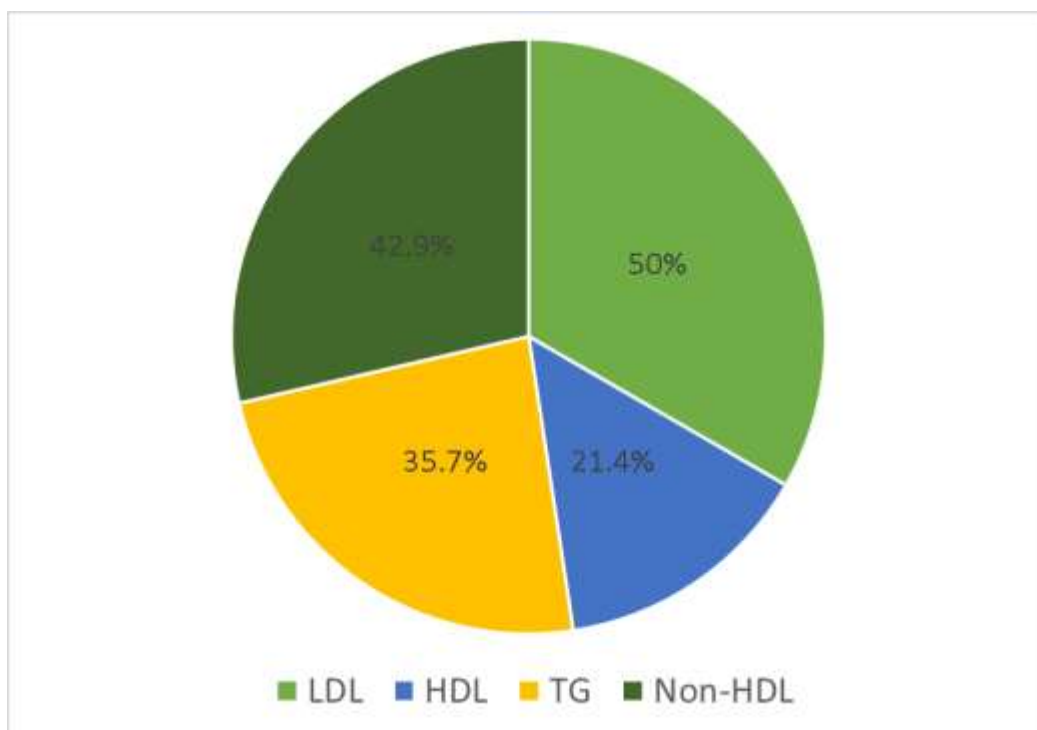


Figure 4 : % of statin respons in 14 case study sample



DISCUSSION

Twenty subjects were recruited for this study the number of males (12) and females (8), The mean age of the patients was 51.45±3.9 years.

In present study, the most prevalent lipid abnormality was HDL 78% above the target (>1.02 mmol/l) followed by TG 64% above target (<1.7 mmol/l), then non-HDL 57% above target (<3.4 mmol/l) & LDL 50% above target level (<2.6 mmol/l).

HDL level is 78% above target in patients use statin in this study similar results in another study done in Maduria College of Medicine in India found that the HDL was 90% above target,⁽¹⁶⁾ less value was in Sarfraz et al in Pakistan found that the HDL was in 70.5% of patients above target.⁽¹⁷⁾

In our study 50% of patients had LDL above target, similar results by American Clinical Chemistry during survey conducted in 2008 found that 49.5% was above target⁽¹⁸⁾ & less than this finding found in study done in Maduria College of Medicine in India found that 10% of LDL is above target.⁽¹⁶⁾

In present study the TG in 64% of patients, found to be above target, less than this finding in study done in Maduria College of Medicine in India found that 45% of patients above target level⁽¹⁶⁾, In Iraq, a survey conducted by WHO in 2015 found that 33.6% of general Iraqi population has triglycerides level 33.6% above target.⁽¹⁹⁾

In our study 57% of patients had non-HDL above target level, Less than this finding is reported by WHO in Iraq 2015 which found that 33.4% of population was above target,⁽¹⁹⁾ The American Clinical Chemistry found high result to our study that about 70.73% above target.⁽¹⁸⁾

The high percentage of lipid profile in our study maybe due to non compliance to treatment, inappropriate dose , dietary habits, lack of physical activity.

Limitations of our study include :sample size, short time ,follow up to patients & patient not know there dose of statin.

CONCLUSIONS

1. The most prevalent abnormality was HDL (78% above the target) followed by TG(64% above the target) then non-HDL (57% above the target) & LDL (50%above target level) .
2. 70% of patient use statin.
3. no one of the patients fulfill in all the targets level.

RECOMMENDATIONS

1. Encourage about the benefit of lipid lowering agent and appropriate use of statin.
2. Emphasize on Non HDL targets to be measured by the doctors and follow the new guide lines for lipid controls .
3. Encourage the patients about life style modification and exercise.
4. We need to decrease the non HDL by encourage exercise, stop smoking eating fish, increase HDL

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RESEARCH QUESTIONNAIRE :

Al-Nahrain University _ College of Medicine / Department of Medicine

Hyperlipidemia in chronic renal failure research questionnaire

- Patient Name : _____.
- Age : () years old.
- Gender () Female () male
- Diagnosis : _____, underlying cause _____.
- Duration : _____.
- Past medical history :
- Drug history :

Investigation:	
- S. Cholesterol	
- S. Triglyceride	
- S. HDL	
- S. LDL	
- S.VLDL	
- Athrogenic index	

